

### **REMARKS**

Reconsideration of this application is respectfully requested. The specification has been amended to remove the incorporation by reference of a European publication. The phrases “and analogues thereof,” “cellulose derivatives,” “silica acid or a derivative or salt thereof,” and “phthalate derivatives” have been removed from claims 1, 27, 28, 41, 51, and 56. Claim 2 has been canceled without prejudice. Claim 41 has been amended to remove the transitional phrase “including.” Claim 42 has been amended to recite that at most 10% w/w of the active ingredient is released within the first 3 hours following administration. *See* page 21, line 32, to page 22, line 2, of the specification. Additionally, claims 1 and 56 have been amended to remove the phrase “and the pharmaceutical composition is free of organic solvent.” Finally, claims 1, 7–10, 22–23, 37 and 44 have been amended to remove the term “about,” when it follows either the term “between,” “from” or “at least.” No new matter has been added by these amendments.

Claims 1, 3–29, 31–34, 36–44 and 51–56 are pending. As claims 12, 38 and 39 have been withdrawn from consideration, claims 1, 3–11, 13–29, 31–34, 36, 37, 40–44 and 51–56 are currently at issue.

### **Objection to the Specification**

The specification has been objected to for incorporating by reference a European publication. The specification has been amended to remove this incorporation by reference. Accordingly, applicants respectfully request withdrawal of this objection.

### **Indefiniteness Rejections**

Claims 1, 3–11, 13–37, 40–44 and 51 have been rejected as indefinite. Specifically, claims 1, 7, 22–23, 37 and 44 have been rejected for including the terms “between about,” “from about,” and “at least about.” The Examiner argues that it is unclear as to what range is covered

because it is unclear whether “between,” “at least,” “from,” or “about” controls the metes and bounds of the respective phrases.

While Applicants respectfully disagree, in order to expedite prosecution of this application, “about” has been deleted from these claims.

Claim 41 has been rejected for reciting the transitional phrase “including” in a Markush group. Claim 41 has been amended to delete the term “including.”

Claim 42 has been rejected since the claim does not recite what is released. Claim 42 has been amended to recite that at most 10% w/w of the active ingredient is released within the first 3 hours following administration. *See* page 21, line 32, to page 22, line 2, of the specification.

For the foregoing reasons, Applicants respectfully request withdrawal of this rejection.

#### **Written Description Rejection**

Claims 1, 3–11, 13–29, 31–34, 36, 37, 40–44, 51, 53, 55 and 56 have been rejected as lacking written description due to the phrase “free of organic solvent.” The Examiner argues that the specification does not provide support for a composition “free of organic solvent.” While Applicants respectfully disagree with the Examiner, this phrase has been removed from the claims in order to expedite prosecution of this application.

Claims 1, 3–11, 13–37, 40–44 and 51 have been rejected as lacking written description due to the phrases “analogues thereof,” “cellulose derivatives,” “silica acid or a derivative or salt thereof,” and “phthalate derivatives.” While Applicants respectfully disagree with the Examiner, these terms have been removed from the claims in order to expedite prosecution of this application.

#### **Obviousness Rejection – U.S. 2003/0180352 (Patel)**

Claims 1, 3–11, 13–29, 31–34, 36, 37, 40–44 and 51–56 have been rejected as obvious over Patel.

In the Advisory Action, the Examiner contends that because both PEG6000 and poloxamer 188 are exemplified in Patel (examples 30 and 31), the combination of the two is obvious. Both of these examples in Patel are directed to lansoprazole formulations, and not an active agent with a low bioavailability of at most 20%, such as tacrolimus (see Application as filed, p.2, ll. 33–37). In contrast to tacrolimus, lansoprazole has an absolute bioavailability of over 80% (*see* Exhibit 1, p. 2). There is no teaching or suggestion in Patel that the combination of PEG and poloxamer would dramatically enhance the bioavailability of the ordinarily low bioavailability drug tacrolimus.

In fact, Patel teaches a formulation of tacrolimus with a PEG-24 cholesterol ether. This formulation is taught in a section (Examples 13–28) of the specification separate from the lansoprazole formulations, which are taught in examples 29–34. Patel teaches that the compositions [of examples 13–28] can

further include additional additives, excipients, and other components for the purpose of facilitating the processes involving the preparation of the composition or the pharmaceutical dosage form, as described herein, as is well-known to those skilled in the art.

(Patel, Paragraph [0417], underlining added). One of ordinary skill in the art, based on this teaching, would not have substituted PEG and poloxamer for the PEG-24 cholesterol ether, he or she would have at best, added additional excipients to the formulation. The Examiner, therefore, appears to be picking and choosing distinct teachings of Patel where there is no motivation to combine any one or more of their respective disclosures into a single claimed embodiment. *ATD Corp. v. Lydall, Inc.*, 159 F.3d 534, 546 (Fed. Cir. 1998) (“Determination of obviousness can not be based on the hindsight combination of components selectively culled from the prior art to fit the parameters of the patented invention.”); *Symbol Technologies, Inc. v. Opticon, Inc.*, 935 F.2d 1569 (Fed. Cir. 1991) (“We do not ‘pick and choose among the individual elements of assorted prior art references to recreate the claimed invention,’ but rather, we look for ‘some teaching or suggestion in the references to support their use in the particular claimed combination.’”).

Furthermore, the presently claimed tacrolimus composition provides significantly superior bioavailability compared to a marketed form of tacrolimus known as Prograf<sup>®</sup>. *See* Example 6 (pages 35 and 36) of the specification. The formulation of the present invention exhibited an area under the curve (AUC) that was more than 7 times that obtained with Prograf<sup>®</sup>, despite the fact that both formulations contained the same amount of tacrolimus. Patel does not disclose or suggest that a tacrolimus formulation containing a vehicle of PEG and poloxamer would exhibit such a significant enhancement in bioavailability.

For the foregoing reasons, Patel does not render obvious the presently claimed invention. Accordingly, applicants respectfully request withdrawal of this rejection.

#### **Double Patenting Rejections**

Claims 1, 3–11, 13–29, 31–34, 36, 37, 40–44 and 51–56 are provisionally rejected for obviousness-type double patenting over claims 1, 6–12, 17–23, 26–32, 34–37, 63 and 64 of copending application 10/513,807. Claims 1, 3–11, 13–29, 31–34, 36, 37, 40–44 and 51–56 are provisionally rejected for obviousness-type double patenting over claims 1–50 of copending application 11/885,992. Applicants request that these provisional rejections in abeyance until a claim is found allowable.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

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Respectfully submitted,

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Enclosures

- Exhibit 1 – PREVACID<sup>®</sup> NDA